Poster III-36

Quantitative Morphometry of Reconstructed Hippocampal Pyramidal Cells: Differences Between Anatomical Subregions and Reconstructing Laboratories

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The dendritic trees of hippocampal pyramidal cells play important roles in the establishment and regulation of network connectivity, synaptic plasticity, and firing dynamics. Several laboratories routinely reconstruct CA3 and CA1 dendrites to correlate their three-dimensional structure with biophysical, electrophysiological, and anatomical observables. To integrate and assess the consistency of the quantitative data available to the scientific community, we analyzed 143 completely reconstructed neurons intracellularly filled and digitized in 5 different laboratories from 10 experimental conditions. Each neuronal group was characterized by an exhaustive array of 148 morphometric parameters. A preliminary exploratory comparison among groups was carried out using a novel machine learning classification algorithms. This algorithm extracted from the high-dimensional parameter space a set of quantitative rules to separate each pair of neuronal groups. The number of false negatives, positives, and of rules required for a given classification were used to define a "distance" between groups. Analysis of these data suggested the presence of significant differences both between anatomical classes (CA3 and CA1) and among different laboratories. The rule-based algorithm not only yielded good classification performance, but also allowed inductive knowledge discovery. In other words, the algorithm output indicated what morphometric parameters best separated between specific groups.

This information was exploited to perform a smaller scale but more rigorous statistical analysis. Thirty morphometric parameters, including most common neuroanatomical measures, were extracted from all neurons and compared between group pairs using Bonferroni-corrected Wilcoxon test. A consistent fraction of parameters (11/30) was significantly different between CA3 and CA1 cells. A considerably large number of parameters was also found that discriminated among neurons within the same morphological class, but reconstructed in different laboratories. These inter-laboratory differences (8/30 parameters) far outweighed the differences between experimental conditions within a single lab, such as aging or preparation method (at most two significant parameters). The set of morphometrics separating anatomical regions and that separating reconstructing laboratories were almost entirely non-overlapping. CA3 and CA1 neurons could be distinguished by global quantities such as branch order and Sholl distance. Differences among laboratories were largely due to local variables such as branch diameter and local bifurcation angles. Only one parameter (a ratio of branch diameters) separated both morphological classes and reconstructing laboratories. Compartmental simulations of electrophysiological activity showed that both differences between anatomical classes and reconstructing laboratories could dramatically affect the firing rate of these neurons under different experimental conditions.

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